510(k) Summary	DAKO Mouse Anti-Human Progesterone Receptor Clone PgR 636	DAKO

K020023

FEB 2 8 2002

Submitter: DAKO Corporation
6392 Via Real
Carpinteria, CA 93013
805-566-6655

Contact: Gretchen M. Murray, Ph.D., Regulatory and Clinical Affairs Manager

Date Summary Prepared: December 18, 2001

Device Name: 1) DAKO® Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Antibody for Immunoenzymatic Staining (Product Code No. M3569)

2) DAKO® Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use Antibody for Immunoenzymatic Staining (Product Code No. N1630)

3) DAKO® Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use Antibody for Immunoenzymatic Staining (Product Code No. NP008)

Device Classification: Class II for prognostic immunohistochemical staining reagents (21 CFR 864.1860).

Panel: Hematology and Pathology Devices Panel, Division of Clinical Laboratory Devices.

Predicate Device: Abbott PR-EIA approved by the FDA as PMA # P900013 and downclassified to Class II by 21 CFR 864.1860, Immunohistochemistry Reagents and Kits on June 3, 1998. Device package insert from this product is included in Section 2 of this submission.

Device Description: 1) Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, (Product Code No. M3569) is a mouse anti-human monoclonal antibody produced as a tissue culture supernatant. The antibody is supplied in 0.05M Tris-HCl buffer, pH 7.2, containing fetal bovine serum and 15mM sodium azide. (0.2 mL and 1 mL total volume).

2) Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use Antibody (Product Code No. N1630) consists of a mouse anti-human monoclonal antibody produced as a tissue culture

supernatant and pre-diluted in 0.05M Tris-HCl buffer, pH 7.6, containing fetal bovine serum and 15mM sodium azide (7mL and 11 mL sizes).

3) Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636, Ready-to-Use Antibody (Product Code No. NP008) consists of a mouse anti-human monoclonal antibody produced as a tissue culture supernatant and pre-diluted in 0.05M Tris-HCl buffer, pH 7.6, containing fetal bovine serum and 15mM sodium azide (7mL total volume).

Intended Use:

For *In Vitro* Diagnostic Use

Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636 is used in the qualitative detection of human progesterone receptor in tissue sections of human breast cancer by immunohistochemistry using a manual or automated procedure. This antibody is indicated for use as an aid in selecting patients most likely to benefit from hormonal therapy as well as an aid in the prognosis and management of breast cancer.

Experimental Data:

Distribution of PgR throughout normal tissue has been reported in a variety of studies. The nuclei of uterine gland cells were found to be strongly immunoreactive. Weaker immunostaining was observed in the nuclei of endometrial and prostatic stromal cells.

Immunoreactivity in a panel of normal tissues:
The required panel of normal tissues was tested with this antibody as specified in the 6/3/98 final version of *Guidance for Submissions of Immunohistochemistry Applications to the FDA.* All tissues were formalin fixed and paraffin embedded. Staining was performed using the DAKO LSAB®2 Peroxidase kit system (Code No. K0672).

Table 1 contains a list of positive tissues with PgR immunoreactivity. All tissues were formalin-fixed and paraffin embedded and stained with Anti-PgR, 636 according to the instructions in the package insert.

TABLE 1: Summary of PgR Normal Tissue Reactivity

TISSUE TYPE (# tested)	POSITIVE TISSUE ELEMENT STAINING AND STAINING PATTERN
Breast (3)	Ductal epithelial cells (3+ staining intensity, 3/3 tissues)
Cervix uteri (3)	Glandular epithelial cells (2+ staining intensity, 1/3 tissues); Stromal fibroblasts(2+ staining intensity, 2/3 tissues)
Pituitary (3)	Pituicytes (2+ staining intensity, 1/3 tissues)
Prostate (3)	Stromal fibroblasts (2+ staining intensity, 1/3 tissues)
Uterus (3)	Endometrial stroma (2+ staining intensity 3/3 tissues) Myometrium (2+ staining intensity, 3/3 tissues) Endometrial glands (2+ staining intensity, 2/3 tissues)

Negative tissues included adrenal (4), bone marrow (2,) brain/cerebellum (4), brain/cerebrum (3), colon (3), esophagus (3), heart (3), kidney (3), liver (3), lung (3), mesothelial cells (3), ovary (3), pancreas (3), parathyroid (3), peripheral nerve (3), salivary gland (3), skeletal muscle (3), skin (3), small intestine (3), spleen (4), stomach (3), testis (3), thymus (3), thyroid (3), and tonsil (3).

A second survey of normal tissues demonstrated positivity in endometrium and weak positivity in prostate after heat-induced epitope retrieval. Negative tissues included esophagus, testes, breast liver, kidney, skeletal muscle, placenta, adrenal, tonsil, lung, colon, skin, pancreas, spleen, thyroid, stomach and cardiac muscle. (See Press article)

Other testing with PgR 636 clone

Western blot

PgR 636 was tested in Western blots using whole cell extracts from 2 cell lines, MDA-MB-231 (PR negative) and T47D (PR A and PR B positive). PgR 636 reacted strongly with both PR-A and PR-B bands from T47D cells, and gave little or no cross reactivity with other proteins in the T47D cell extracts. PgR 636 reacted equally with unliganded and liganded PR. The domain mapping experiments demonstrated that PgR 636 reacted with amino terminal domain (AN) and the amino terminal domain linked to DBD, but not with any of the C-terminal tail (aa 919-933) of human PR. Thus, the PgR 636 epitope is contained within the amino termal domain common to the A and B receptors in a region between aa 165 and 533. (See Press article)

Immunohistochemistry of tumors

PR 636 was used to immunostain a variety of 60 different tumor types. Breast cancer (5/11), uterine (2/2), ovarian (2/6), and endometrial (2/2) carcinomas stained strongly. Medullary carcinoma of the thyroid (1/2) and testicular yolk sac tumor were positive. Other tumors including

melanoma, lymphoma and neuroendocrine and neural tumors were negative for PR expression. (See Press article)

Comparison testing to Abbott PR-EIA

Substantial equivalence to the Abbott PR-EIA was demonstrated in a comparison study of breast carcinomas. One hundred six tests were performed on 101 specimens previously evaluated for PR presence using the Abbott PR-EIA. Two specimens had too little tumor tissue for evaluation. Two specimens had no corresponding PR-EIA result. Results for the 97 specimens indicated 53 as negative for PR by IHC, and 44 positive. Correlation with the PR-EIA is presented in Table 2.

Table2: Concordance of DAKO Monoclonal Mouse anti-human Progesterone Receptor clone PgR 636 with Abbott PR-EIA

	Abbott Result		
DAKO Result	Negative	Positive	Total
Negative	47	6	53
Positive	3	41	44
Total	50	47	97

Concordance calculation showed concordance = 88 / 97 = 90.7% in this trial. Using the PR-EIA as the predicate device, sensitivity was determined to be 41/47 = 87.2% while specificity was determined to be 47/50, = 94%. The Kappa statistic indicated a 0.8139 kappa, which corresponds to an almost perfect correlation for the qualitative assessment.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Gretchen M. Murray, Ph.D.
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Carpinteria, California 93013

FEB 2 8 2002

Re: k020023
Trade/Device Name: DAKO Monoclonal Mouse Anti-Human Progesterone Receptor, Clone PgR 636 Antibody for Immunoenzymatic Staining available in three different iterations:
1. (Product Code No. M3569),
2. Ready-to-use (Product Code No. N1630),
3. Ready-to-use (Product Code No. NP008)
Regulation Number: 21 CFR § 864.1860
Regulation Name: Immunohistochemistry Reagents and Kits
Regulatory Class: II
Product Code: MXZ
Dated: December 31, 2001
Received: January 3, 2002

Dear Dr. Murray:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K020023

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The clinical interpretation of any positive staining or its absence should be complemented by morphological and histological studies with proper controls. Evaluations should be made within the context of the patient's clinical history and other diagnostic tests by a qualified individual having knowledge of all the potential antibody reactivities.

PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ (Per 21 CFR 801.109) OR **Over-The-Counter Use**____ (Per 21 CFR 801.110

IVD Use____ (Per 21 CFR 801.119)

Susan S. Alfaro

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K020023